

D2 cont. activity or function as a result of uniform sequence. Such characteristics will typically be measured by way of binding with a selected ligand or receptor.--

Amendments to the specification are indicated in the attached "Marked Up Version of Amendments" (page i-v).

In the Claims

Please amend Claims 172, 183, 185-193, 195, 205 and 206. Amendments to the claims are indicated in the attached "Marked Up Version of Amendments" (pages vi - x).

- D3
172. (Amended) A method of synthesizing a polypeptide array, wherein said array comprises at least two polypeptides, which differ in composition, immobilized on a substrate, said method comprising:
- (a) contacting a surface of the substrate with a first protected amino acid wherein said first protected amino acid is selectively coupled to a functional group selected from the group consisting of:
 - (i) a functional group attached to the substrate;
 - (ii) a functional group attached to a linker that is attached to the substrate;
 - (iii) a functional group attached to an amino acid that is coupled to the substrate;
 - (iv) a functional group attached to an amino acid that is coupled to a linker that is attached to the substrate;
 - (v) a functional group attached to a nascent polypeptide that is coupled to a linker that is attached to the substrate;
 - (vi) a functional group attached to a nascent polypeptide coupled to the substrate; and
 - (vii) combinations thereof,wherein the functional group is in a first selectively activated region of said surface, and wherein a protecting group has been removed from said first

selectively activated region of the surface without removing protecting groups from other positionally defined locations of the substrate;

- (b) contacting said surface with a second protected amino acid wherein said second protected amino acid is selectively coupled to a functional group selected from the group consisting of:

- (i) a functional group attached to the substrate;
- (ii) a functional group attached to a linker that is attached to the substrate;
- (iii) a functional group attached to an amino acid that is coupled to the substrate;
- (iv) a functional group attached to an amino acid that is coupled to a linker that is attached to the substrate;
- (v) a functional group attached to a nascent polypeptide that is coupled to a linker that is attached to the substrate;
- (vi) a functional group attached to a nascent polypeptide coupled to the substrate; and
- (vii) combinations thereof,

wherein the functional group is in a second selectively activated region of said surface, and wherein a protecting group has been removed from said second selectively activated region of the surface without removing protecting groups from other positionally defined locations of the substrate; and,

- (c) repeating the above steps until at least two polypeptides, which differ in composition, are formed at positionally defined locations on said substrate surface.

183. (Amended) A method for synthesizing polypeptides on a substrate, said method comprising:

- a) providing a substrate wherein said substrate comprises immobilized polypeptide molecules, said polypeptide molecules coupled to a removable protecting group;

- DA
cont.
- b) removing said protecting group from said polypeptide molecules in a first positionally defined location of said substrate without removing said protecting groups from a second positionally defined location of said substrate; and
 - c) contacting said substrate with a first amino acid to couple said first amino acid to said polypeptide molecules in said first positionally defined location, said first amino acid having an amino acid protecting group thereon, forming a first polypeptide on said substrate in said positionally defined location that is different in composition from a polypeptide in said second positionally defined location.
-

- DS
- 185. (Amended) The method as recited in claim 184, wherein said irradiation step is a step of masking a light source with a mask placed between said light source and said substrate, said mask comprising first transparent regions and second opaque regions, said transparent regions transmitting light from said source to at least said first positionally defined location, and said opaque regions blocking light from said source to at least said second positionally defined location.
 - 186. (Amended) The method as recited in claim 183, wherein said first and second positionally defined location each have total areas less than about 1 cm².
 - 187. (Amended) The method as recited in claim 184, wherein said irradiation steps are conducted with a monochromatic light.
 - 188. (Amended) The method as recited in claim 184, wherein said irradiation steps and contacting are repeated so as to synthesize 10³ different polypeptides on said substrate.
 - 189. (Amended) The method as recited in claim 184, wherein the irradiation step for a first positionally defined location is a step of irradiating half of a positionally defined location of said substrate irradiated in a prior synthesis step, and not irradiating half of said positionally defined location irradiated in a prior synthesis step.

190. (Amended) The method as recited in claim 183, wherein said steps a) and b) are repeated to synthesize more than 1,000 different polypeptides on different synthesis locations of said substrate, each of said different polypeptides occupying an area of less than about 10^{-2} cm^2 to about $1 \times 10^{-5} \text{ cm}^2$.

15
cont.
191. (Amended) The method as recited in claim 190, wherein said steps a) and b) are repeated to synthesize more than 1,000 different polypeptides on different synthesis locations of said substrate, each of said different polypeptides occupying an area of less than about 10^{-2} cm^2 to about $1 \times 10^{-4} \text{ cm}^2$.

192. (Amended) The method as recited in claim 191, wherein said steps a) and b) are repeated to synthesize more than 1,000 different polypeptides on different synthesis locations of said substrate, each of said different polypeptides occupying an area of less than about 10^{-2} cm^2 to about $1 \times 10^{-3} \text{ cm}^2$.

193. (Amended) A method of synthesizing polypeptides, said method comprising:

- a) generating a pattern of light and dark areas by selectively irradiating at least a first area of a surface of a substrate, said surface comprising immobilized amino acids on said surface, said amino acids coupled to a photoremovable protective group, without irradiating at least a second area of said surface, to remove said protective group from said amino acids in said first area;
- b) simultaneously contacting said first area and said second area of said surface with a first amino acid to couple said first amino acid to said immobilized amino acids in said first area, and not in said second area, said first amino acid having said photoremovable protective group;
- c) generating another pattern of light and dark areas by selectively irradiating with light at least a part of said first area of said surface and at least a part of said second area to remove said protective group in said at least a part of said first area and said at least a part of said second area;

- D5
cont,
- d) simultaneously contacting said first area and said second area of said surface with a second amino acid to couple said second amino acid to said immobilized amino acids in at least a part of said first area and at least a part of said second area; and
- e) performing additional irradiating and amino acid contacting and coupling steps so that a matrix array of at least 100 polypeptides, which differ in composition, is formed on said surface, each different polypeptide synthesized in an area of less than 0.1 cm^2 , whereby said different polypeptides have sequences and locations on said surface defined by the patterns of light and dark areas formed during the irradiating steps and the amino acids coupled in said contacting steps.
-

- D6
195. (Amended) The method as recited in claim 193, wherein said protective group is one or more protective groups selected from the group consisting of 6-nitroveratryloxycarbonyl, 2-nitrobenzyloxy carbonyl, dimethyl dimethoxybenzyloxy carbonyl, 5-bromo-7-nitroindolyl, o-hydroxyalpha-methyl cinnamoyl, and 2-oxymethylene anthriquinone.
-

- D7
205. (Amended) The method as recited in claim 204, wherein said additional steps are performed so as to synthesize 10^3 different polypeptides in 10^3 respective positionally defined locations on said substrate.

206. (Amended) The method as recited in claim 204, wherein said additional steps are performed so as to synthesize 10^6 different polypeptides in 10^6 respective positionally defined locations on said substrate.
-

REMARKS

I. Supplemental Information Disclosure Statement

A Supplemental Information Disclosure Statement (SIDS) is being filed concurrently herewith. Entry of the SIDS is respectfully requested.